

CLAIMS

We claim:

1. A thermogelling biodegradable aqueous polymer solution, comprising:
 - a. a biodegradable polymer, comprising
 - i. a polyethylene glycol (PEG) block, and
 - ii. a biodegradable polyester block, wherein
 - iii. said blocks are linked to form a polymer of a general structure comprising the formula of $A_n(B)$, where n is greater than 2 and A is selected from the group consisting of a polyethylene glycol block and a biodegradable polyester block, B is selected from the group consisting of a polyethylene glycol block and a biodegradable polyester block, and A is different from B ; and
 - b. an aqueous solution.
2. A thermogelling biodegradable aqueous polymer solution according to claim 1 wherein n is between 3 and 10.
3. A thermogelling biodegradable aqueous polymer solution according to claim 1 wherein said polyethylene glycol (PEG) has an average molecular weight of between about 300 and 20,000.

4. A thermogelling biodegradable aqueous polymer solution according to claim 1 wherein said polyethylene glycol (PEG) has an average molecular weight of between about 500 and 10,000.

5. A thermogelling biodegradable aqueous polymer solution according to claim 1 wherein said polyester block has an average molecular weight of between about 1,000 and 30,000.

6. A thermogelling biodegradable aqueous polymer solution according to claim 1 wherein said polyester block has an average molecular weight of between about 1,000 and 10,000.

7. A thermogelling biodegradable aqueous polymer solution according to claim 1, wherein said biodegradable polyester block is selected from the group consisting of poly(DL-lactic acid), poly(L-lactic acid), poly(glycolic acid), poly(ϵ -caprolactone), poly(γ -butyrolactone), poly(γ -valerolactone), poly(β -hydroxybutyric acid), and their copolymers or terpolymers.

8. A thermogelling biodegradable aqueous polymer solution according to claim 7, wherein said copolymers and/or terpolymers are selected from the group consisting of poly(DL-lactic acid-co-glycolic acid), poly(L-lactic acid-co-glycolic acid), poly(ϵ -caprolactone-co-DL-lactic acid), copoly(ϵ caprolactone co DL lactic acid glycolic acid).

9. A biodegradable bioactive agent delivery system, comprising:
a. an effective amount of bioactive agent contained in;

b. a thermogelling biodegradable aqueous polymer solution comprising

i. A biodegradable polymer, comprising a polyethylene glycol (PEG) block a biodegradable polyester block, wherein said blocks are linked to form a polymer of a general structure comprising the formula of $A_n(B)$, where n is greater than 2 and A is selected from the group consisting of a polyethylene glycol block and a biodegradable polyester block, B is selected from the group consisting of a polyethylene glycol block and a biodegradable polyester block, and A is different from B, and

ii. an aqueous solution.

10. A biodegradable bioactive agent delivery system according to claim 9 wherein said bioactive agent is a drug.

11. A biodegradable bioactive agent delivery system according to claim 10 wherein said drug is selected from the group consisting of anti-cancer agents, hormones, antibiotics, narcotic antagonists, analgesics, anti-inflammatory agents, anti-depressants, anti-epileptics, anti-malarial agents, immunoactivators, growth factors, radioprotection agents, vaccines, gene therapy agents, oligonucleotides, antisense, peptides and proteins, and combinations thereof.

12. A biodegradable bioactive agent delivery system according to claim 10 wherein said drug is an anti-cancer agent.

13. A biodegradable bioactive agent delivery system according to claim 12 wherein said anti-cancer agent is a member selected from the

carboplatin, doxorubicin, daunorubicin, 5-fluorouracil, methotrexate, taxol, taxotere, and actinomycin D.

14. A biodegradable bioactive agent delivery system according to claim 10 wherein said drug is a polypeptide.

15. A biodegradable bioactive agent delivery system according to claim 14 wherein said polypeptide is a member selected from the group consisting of oxytocin, vasopressin, adrenocorticotrophic growth factor (PDGF), prolactin, luteinizing hormone releasing hormone (LHRH), growth hormone, growth hormone releasing factor, insulin, somatostatin, glucagons, interleukin-2 (IL-2), interferon- α, β, γ (IFN- α, β, γ), gastrin, tetragastrin, pentagastrin, urogastroin, secretin, calcitonin, enkephalins, endorphins, angiotensins, thyrotropin releasing hormone (TRH), tumor necrosis factor (TNF), nerve growth factor (NGF), granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (M-CSF), rennin, bradykinin, bacitracins, alpha-1 antitrypsin, platelet derived growth factor, albumin, anti-thrombin III, glucocerebrosidase, DNase, tissue plasminogen activator, calcitonin, clotting factors VII, VIII, and IX, LHRH antagonists, insulin, erythropoietin, polymyxins, colistins, tyrocidin, gramicidins, and synthetic analogues, modifications and pharmacologically active fragments thereof, monoclonal antibodies and soluble vaccines.

16. A biodegradable bioactive agent delivery system according to claim 9 wherein said therapeutic agent is a cell.

17. A biodegradable bioactive agent delivery system according to claim 9 wherein said thermogelling biodegradable aqueous polymer solution provides as a solubilizer.

18. A method for the parenteral delivery of a bioactive agent in a thermogelling polymer matrix to a warm blooded animal for the controlled release of said bioactive agent, which comprises:

- a. providing an injectable thermogelling biodegradable aqueous polymer solution, which comprises
 - i. A biodegradable polymer, comprising a polyethylene glycol (PEG) block, a biodegradable polyester block, wherein said blocks are linked to form a polymer of a general structure comprising the formula of $A_n(B)$, where n is greater than 2 and A is selected from the group consisting of a polyethylene glycol block and a biodegradable polyester block, B is selected from the group consisting of a polyethylene glycol block and a biodegradable polyester block, and A is different than B , and
 - ii. an aqueous solution;
- b. mixing said thermogelling biodegradable aqueous polymer solution with an effective amount of bioactive agent to form a polymer-bioactive agent mixture;
- c. maintaining said polymer-bioactive agent mixture at a temperature below the gelling temperature of said polymer; and
- d. injecting said solution parenterally into said warm blooded animal forming a gel depot of said bioactive agent and biodegradable polymer as the temperature of the solution is raised by the body temperature of said animal to be above the gelling temperature of said polymer.

19. A method according to claim 18 wherein said bioactive agent is a drug.

20. A method according to claim 19 wherein said drug is an anti-cancer agent.

21. A method according to claim 20 wherein said anti-cancer agent is a member selected from the group consisting of adriamycin, mitomycin, bleomycin, cisplatin, carboplatin, doxorubicin, daunorubicin, 5-fluouroacil, methotrexate, taxol, taxotere, and actinomycin D.

22. A method according to claim 19 wherein said drug is a polypeptide.

23. A method according to claim 22 wherein said polypeptide is a member selected from the group consisting of oxytocin, vasopressin, adrenocorticotrophic growth factor (PDGF), prolactin, luliberin or luteinising hormone releasing hormone (LHRH), growth hormone, growth hormone releasing factor, insulin, somatostatin, glucagons, interleukin-2 (IL-2), interferon- α, β, γ (IFN- α, β, γ), gastrin, tetragastrin, pentagastrin, urogastroine, secretin, cacitonin, enkephalins, endorphins, angiotensins, thyrotropin releasing hormone (TRH), tumor necrosis factor (TNF), nerve growth factor (NGF), granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (M-CSF), rennin, bradykinin, bacitracins, alpha-1 antitrypsin, platelet derived growth factor, albumin, anti-thrombin III, glucocerebrosidase, DNase, tissue plasminogen activator, calcitonin, clotting factors VII, VIII, and IX, LHRH antagonists, insulin, erythropoietin, polymixins, colistins, tyrocidin,

pharmacologically active fragments thereof, monoclonal antibodies and soluble vaccines.

24. A method for the delivery of a bioactive agent in a thermogelling polymer matrix to a warm blooded animal for the controlled release of said bioactive agent, which comprises:

a. providing a thermogelling biodegradable aqueous polymer solution, which comprises

i. A biodegradable polymer, comprising a polyethylene glycol (PEG) block, a biodegradable polyester block, wherein said blocks are linked to form a polymer of a general structure comprising the formula of $A_n(B)$, where n is greater than 2 and A is selected from the group consisting of a polyethylene glycol block and a biodegradable polyester block, B is selected from the group consisting of a polyethylene glycol block and a biodegradable polyester block, and A is different than B , and

ii. an aqueous solution;

b. mixing said thermogelling biodegradable aqueous polymer solution with an effective amount of bioactive agent to form a polymer-bioactive agent mixture;

c. maintaining said polymer-bioactive agent mixture at a temperature below the gelling temperature of said polymer; and

d. providing said polymer-bioactive agent mixture into said warm blooded animal forming a gel depot of said bioactive agent and biodegradable polymer as the temperature of the liquid is raised by the body temperature of said animal to be above the gelling temperature of said polymer.

25. A method according to claim 24 wherein said bioactive agent is a drug.

26. A method according to claim 25 wherein said drug is selected from the group consisting of anti-cancer agents, hormones, antibiotics, narcotic antagonists, analgesics, anti-inflammatory agents, anti-depressants, anti-epileptics, anti-malarial agents, immunoactivators, growth factors, radioprotection agents, vaccines, gene therapy agents, oligonucleotides, antisense, peptides and proteins, and combinations thereof.

27. A method according to claim 25 wherein said drug is an anti-cancer agent.

28. A method according to claim 27 wherein said anti-cancer agent is a member selected from the group consisting of adriamycin, mitomycin, bleomycin, cisplatin, carboplatin, doxorubicin, daunorubicin, 5-fluorouracil, methotrexate, taxol, taxotere, and actinomycin D.

29. A method according to claim 25 wherein said drug is a polypeptide.

30. A method according to claim 29 wherein said polypeptide is a member selected from the group consisting of oxytocin, vasopressin, adrenocorticotrophic growth factor (PDGF), prolactin, luteinising hormone releasing hormone (LHRH), growth hormone, growth hormone releasing factor, insulin, somatostatin, glucagons, interleukin-2 (IL-2), interferon- α, β, γ (IFN- α, β, γ), gastrin, tetragastrin, pentagastrin,

thyrotropin releasing hormone (TRH), tumor necrosis factor (TNF), nerve growth factor (NGF), granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (M-CSF), rennin, bradykinin, bacitracins, alpha-1 antitrypsin, platelet derived growth factor, albumin, anti-thrombin III, glucocerebrosidase, DNase, tissue plasminogen activator, calcitonin, clotting factors VII, VIII, and IX, LHRH antagonists, insulin, erythropoietin, polymyxins, colistins, tyrocidin, gramicidines, and synthetic analogues, modifications and pharmacologically active fragments thereof, monoclonal antibodies and soluble vaccines

31. A biodegradable polymer, comprising:

- a. a polyethylene glycol (PEG) block; and
- b. a biodegradable polyester block, wherein;
- c. said blocks are linked to form a polymer of a general

structure comprising the formula of $A_n(B)$, where n is greater than 2 and A is selected from the group consisting of a polyethylene glycol block and a biodegradable polyester block, B is selected from the group consisting of a polyethylene glycol block and a biodegradable polyester block, and A is different from B .